IN THE UNITED STATES DISTRICT COURT
FOR THE WESTERN DISTRICT OF TENNESSEE
WESTERN DIVISION

PATRICIA NOZINICH and PETER NOZINICH, **Plaintiffs,** **vs.** **JOHNSON & JOHNSON, INC., and CENTOCOR, INC.,** **Defendants.**	**Case No. 2:09-CV-02105-DKV**

DEFENDANTS' MEMORANDUM OF LAW IN RESPONSE TO PLAINTIFFS' MOTION FOR PARTIAL SUMMARY JUDGMENT OR IN THE ALTERNATIVE MOTION TO STRIKE LEARNED INTERMEDIARY DEFENSE

Defendants Centocor Ortho Biotech, Inc. and Johnson & Johnson, Inc. (collectively, "Centocor") respectfully submit this Response to Plaintiffs' Motion for Partial Summary Judgment , or in the Alternative, Motion to Strike Learned Intermediary Defense ("Plaintiffs' Motion"), and memorandum in support thereof (Doc. 87) filed on April 7, 2011. In response to Plaintiffs' Motion, Centocor respectfully states as follows:

PRELIMINARY STATEMENT

Plaintiffs have employed a "kitchen sink" strategy in their partial summary judgment motion. Their motion consists of the *ipse dixit* of counsel, incorrect and misleading citations to irrelevant documents, unsupported statements represented to be indisputable facts, and demonstrably incorrect allegations about how the prescriber here, Dr. Judy Ash, made her decision to recommend Remicade® for Patricia Nozinich. None of plaintiffs' arguments

establish an undisputed material fact. Moreover, plaintiffs have misstated applicable Tennessee law and mischaracterized the law in other states concerning the "learned intermediary" doctrine.

For all the reasons why defendants' summary judgment motion should be granted, plaintiffs' partial motion should be denied.

STATEMENT OF FACTS

The facts regarding the history of the marketing of Remicade® as it relates to the medicine's labeling and the evaluation of post-marketing information regarding reports of possible thromboembolic events are set forth in Centocor's summary judgment motion (*See* Defendants' Statement of Undisputed Material Facts In Support of Their Motion for Summary Judgment filed on April 7, 2011 (Dkt. Entry No. 86-6), ¶¶ 1-8 ("Defendants' SUF")) and will not be repeated here.

With respect to plaintiffs' allegations about "MedWatch" reports and Periodic Safety Update Reports ("PSURs") (*see* Plaintiffs' Statement of Material, Undisputed Facts filed on April 7, 2011 (Dkt. Entry No. 87-1), ¶¶ 45-63 (hereinafter "Plaintiffs' SUF")), Centocor submits the relevant, material facts are as follows:

The Remicade® package insert is a comprehensive document that contains "the most salient data, efficacy and safety," which includes post-marketing data. (Feb. 8, 2011 Deposition of Dr. Suzanne Travers, M.D. ("Travers Dep."), 189:2-16; 192:15-17, Dkt. Entry No. 81, excerpts attached hereto as **Exhibit A**). Remicade® post-marketing adverse events are reported to Centocor from worldwide sources and are entered in the Company's safety database called SCEPTRE. Id., 34:17-36:20, 41:5-13, 104:4-5). SCEPTRE also contains serious adverse events reported in clinical trials and medical publications. (Id., 35:4-5, 36:3-12, 41:5-13). All the post-marketing data that is collected on individual adverse event reports is added to

SCEPTRE. (Id., 74:14-21). Each report is submitted to the United States Food & Drug Administration ("FDA") on what is known as a MedWatch report. (Id. 74:2-6).

"MedWatch" reports are one of the three types of reports in FDA's post-marketing adverse event report ("AER") database.[1] MedWatch is an entirely voluntary program introduced by FDA in 1993. *See* David A. Kessler, "Introducing MEDWatch: A New Approach to Reporting Medication and Device Adverse Effects and Product Problems," 269 JAMA 2765, 2767 (1993); "What is MedWatch?", available at http://www.fda.gov/Safety/MedWatch/HowToReport/default.htm (last visited May 5, 2011). Healthcare professionals and, less frequently, consumers submit MedWatch reports directly to FDA or to manufacturers.[2] *See* "MedWatch Reporting by Consumers," available to http://www.fda.gov/medwatch/report/consumer/consumer.htm (last visited Nov. 16, 2006); "Voluntary Reporting by Health Professionals"," available at http://www.fda.gov/medwatch/report/hcp.htm (last visited May 5, 2011); *In re Meridia Prods. Liab. Litig.*, 328 F. Supp. 2d 791, 807 (N.D. Ohio 2004), *aff'd, Meridia Prods. Liab. Litig. v. Abbott Labs.*, 447 F.3d 861 (6th Cir. 2006). Reporting parties need only fill out a one-page form and mail, fax, or email it to FDA. "Voluntary Reporting by Health Professionals." Reporting by telephone also is available. *Id.*

Since 1999, Centocor has submitted Periodic Safety Update Reports ("PSURs") to FDA. (Feb. 7, 2011 Deposition of Stella Jones, Ph.D. ("Jones Dep."), 31:9-10, Dkt. Entry No. 101, excerpts attached hereto as **Exhibit B**). Data from MedWatch reports, clinical trials, medical publications, registries and any other source of safety information are included and

[1] The other two types are: (1) periodic reports; and (2) 15-day alert reports.

[2] If a MedWatch report is submitted to a manufacturer, the manufacturer is required by law to submit the report to FDA. *See, e.g.*, 21 C.F.R. § 314.80 (2006).

assessed in Centocor's PSURs. (*Id*., 33:1-16). The Remicade® labeling reflects data from SCEPTRE, which includes data from the PSURs and MedWatch reports submitted to FDA. (Travers Dep., 36:21-37:19, 39:5-40:4; Jones Dep., 43:20-22). Data in Remicade® PSURs show that the incidence of pulmonary embolism in post-marketing use of the medicine is low and has not increased over time. (Mar. 23, 2011 Deposition of Dr. Barbara Matthews, M.D. ("Matthews Dep."), 95:1-96:10, 127:6-21, Dkt. Entry No. 91, excerpts attached hereto as **Exhibit C**).

In April 2010, FDA approved the removal of pulmonary embolism as an adverse event from the Remicade® package insert, in compliance with FDA's guidance document for labeling of the adverse events section. After considering the necessary factors – seriousness of the event, number of adverse event reports and strength of the causal relationship to the medication – FDA concluded that pulmonary embolism no longer met the necessary criteria to be included as an adverse event in the prescribing information for Remicade®. (Defendants' SUF, ¶ 8.) FDA took pulmonary embolism out of the package insert in 2010 after reviewing its own safety database, PSURs and the safety data of other anti-TNF therapies. (Matthews Dep., 102:15-103:13, 127:21-128:5). The removal of pulmonary embolism from the Remicade® prescribing information was based on "thrombosis data review" in PSURs. The data indicated that pulmonary embolism was not an adverse drug reaction associated with Remicade®. (*See* CE02188224-26, CE02188215-23, CE02243147-201, attached to Defendants' Notice of Filing Centocor Documents Under Seal, collectively, as **Exhibit D**, filed concurrently herewith).

With regard to Dr. Ash's knowledge and understanding about Remicade®, she was aware of the reports of pulmonary embolism and the reports of thromboembolic events associated with Remicade® at the time she prescribed the medicine to Ms. Nozinich. (*See* November 30, 2010 Deposition of Judy D. Ash, M.D. ("Ash Dep."), 35:22-36:19; 68:1-5, Dkt.

Entry No. 96, excerpts attached hereto as **Exhibit E**). The undisputed evidence establishes that Dr. Ash was aware of the reports of thromboembolic events (including pulmonary embolism) and, because the occurrence of pulmonary embolism was so low in patients being treated with Remicade®, she independently decided not to share this information with Ms. Nozinich (verbally as in her written Remicade® consent form) prior to treating her with Remicade®. (Ash Dep., 36:6-24)

Based on her knowledge of Remicade®, Dr. Ash exercised her independent clinical judgment in prescribing the medicine to Ms. Nozinich to alleviate the symptoms of her rheumatoid arthritis. (*Id.*) Remicade® was prescribed properly to Ms. Nozinich by Dr. Ash and she was benefitting from the medicine as the symptoms of her disease were improving after the infusions. (*Id.*, 14-22) Dr. Ash did not actually rely on any marketing representations or alleged concealments made by Centocor when prescribing Remicade® to Ms. Nozinich. (*Id.*, 35:22-36:19) Dr. Ash was not influenced at any seminars, presentations, or through literature provided by Centocor regarding Remicade®. To the contrary, plaintiffs' evidence is that Dr. Ash never compromised on patient safety and only prescribed a medicine if it was in her patient's best interests. (Mar. 17, 2009 Deposition of Dr. Gary F. Trew ("Trew Dep."), 36:15-38:7, 115:21-116:14, 120:5-21, Dkt. Entry No. 81, excerpts attached hereto as **Exhibit F**).

Physicians are provided with safety information from Centocor that is derived from the package insert, reports in SCEPTRE and PSURs. (Travers Dep., 46: 11-19). Physicians regularly inquire of Centocor for information on suspected adverse events possibly associated with Remicade®. Centocor's Medical Affairs Department prepares responses to these requests based on the PSURs and data in SCEPTRE. (*Id.*, 47:7-19; 192:18-22). The Medical

Affairs letter that Dr. Ash received regarding pulmonary embolism incorporated post-marketing safety information from the Remicade® package insert and PSURs. (*Id.*, 50:9-14, 53:6-17).

Like every other company, Centocor developed plans to market or promote its products, including Remicade®. All of the marketing activities for Remicade® are closely regulated by FDA and a "guiding principle" of Centocor's marketing efforts was to "comply with all applicable laws and regulations. (CE01886584-683 at CE01886595, *see* Plaintiffs' Notice of Filing Centocor Documents filed on April 7, 2011, Dkt. Entry No. 90, **Filed Under Seal**). None of the Remicade® marketing activities influenced Dr. Ash and plaintiffs did not see any Remicade® advertisements, brochures or videos prior to Dr. Ash recommending Remicade®. (Trew Dep. 36:15-38:7; 115:21-116:14; 120:5-:21; Ash Dep., 22:11-28:2; 40:17-41:14; 47:5-50:16). Any materials Ms. Nozinich received were provided to her in the context of the physician-patient relationship and not in a direct-to-consumer context. (Feb. 22, 2010 Deposition of Patricia Nozinich ("Nozinich Dep."), 52:6-9, 53:10-14, Dkt. Entry No. 78, excerpts attached hereto as **Exhibit G**).

Centocor receives inquiries from FDA and other health regulatory authorities on a regular basis. Swiss Medic, FDA's counterpart in Switzerland, made a request for information regarding pulmonary embolism reports possibly associated with the administration of Remicade® in May 2006. Centocor responded to this request, relying on data including MedWatch reports, that were collected and analyzed in PSURs. The report sent to SwissMedic provided a cumulative summary of thromboembolic events that had been reported in PSURS. (CE00255306-13 at CE00255309 (Table 2), *see* Plaintiffs' Notice of Filing Centocor Documents filed on April 7, 2011, Dkt. Entry No. 90, **Filed Under Seal**). This information was the same PSUR analysis provided to FDA and other health authorities and contained important safety

information described in the Remicade® package insert. (Travers Dep., 36:21-37:19, 39:5-40:4, 46: 11-19, 74:2-6; Jones Dep., 31:9-10, 33:1-16, 43:20-22).

As made clear in the conclusion of Centocor's submission, the message and analysis provided to Swiss Medic and Dr. Ash about the thromboembolic events, including pulmonary embolism, and the administration of Remicade® were the same. (CE00255309, *see* Plaintiffs' Notice of Filing Centocor Documents filed on April 7, 2011, Dkt. Entry No. 90, **Filed Under Seal**)

ARGUMENT

I. THE STANDARDS APPLICABLE TO PLAINTIFFS' MOTION

Plaintiffs' partial summary judgment motion ignores three basic Rule 56 tenets: one, a summary judgment motion must be based on facts, not unsupported assertions of counsel, *see Lujan v. Nat'l Wildlife Fed'n*, 497 U.S. 871, 888 (1990); *see also Laurence v. Gateway Health System*, No. 3:06-0636, 2008 WL 2097390, at *4 (M.D. Tenn. May, 16, 2008), *aff'd.*, 2010 WL 841176 (6th Cir.), *cert. denied*, 131 S.Ct. 418 (2010) ("[C]conclusory allegations, speculation, and unsubstantiated assertions are not evidence, and are not sufficient to defeat a well-supported motion for summary judgment.") (citation omitted); two, the facts must be admissible and not subject to exclusion, *see Stipkala v. Am. Red Cross*, 215 F.3d 1327, 2000 WL 712378, at *6 (6th Cir. May 23, 2000); *Moore v. Holbrook*, 2 F.3d 697, 699 (6th Cir. 1993); *see also Conde v. Velsicol Chem. Corp.*, 804 F. Supp. 972, 992 (S.D. Ohio 1992) ("Affidavits may be properly considered only if the material in the affidavit would be admissible at trial.") (citation omitted), *aff'd*, 24 F.3d 809 (6th Cir. 1994); and three, the facts must be "material" which means they must be relevant and undisputed linked to the issues that must be litigated in the case, *see Anderson v. Liberty Lobby*, 477 U.S. 242, 248 (1986); *Conde*, 804 F. Supp. at 992.

With respect to their violation of Tenet No. 1, plaintiffs' statement is a series of unsupported representations of counsel that are not supported by admissible evidence. For example, plaintiffs imply that Dr. Ash was not apprised of information contained in PSURs. (Plaintiffs' SUF ¶¶44, 46, 47.) However, the evidence is entirely to the contrary. Data in the PSURs always is reflected in labeling and in other communications sent to physicians. (Travers Dep., 36:21-37:19, 39:5-40:4, 46: 11-19, 74:2-6; Jones Dep., 31:9-10, 33:1-16, 43:20-22).

With regard to their violation of Tenet No. 2, several of plaintiffs' "facts" related to interactions between Centocor and "SwissMedic" – a foreign health regulatory authority. (Plaintiffs' SUF, ¶¶ 50-55) Pursuant to settled Sixth Circuit law, interactions with foreign regulators regarding a pharmaceutical are inadmissible in products liability cases. *See Meridia*, 447 F.3d at 867. Therefore, documents concerning these activities cannot be considered in the summary judgment context. *See Conde*, 804 F. Supp. at 992.

With respect to their violation of Tenet No. 3, all of plaintiffs' marketing allegations (Plaintiffs' SUF, ¶¶ 1-16) have nothing to do with Dr. Ash or her decision to prescribe Remicade® for Ms. Nozinich. Accordingly, they have no bearing on this case and, therefore, cannot support plaintiffs' motion or be a reason for denying Centocor summary judgment. *See Laurence*, 2008 WL 2097390, at *4.

II. THE "LEARNED INTERMEDIARY" DOCTRINE APPLIES TO THIS CASE

A. Tennessee recognizes the learned intermediary doctrine, without a direct-to-consumer exception.

1. The learned intermediary doctrine applies in Tennessee

Plaintiffs assert that Tennessee should not apply the learned intermediary doctrine in cases when prescription drug manufacturers market directly to consumers. (Pls.' Mem. In

Supp. of Their Mot. for Partial Summ. J. or in the Alternative Mot. to Strike the Learned Intermediary Defense 19–21, Dkt. Entry 87-14.) However, Tennessee has followed the learned intermediary doctrine without a direct-to-consumer exception for more than twenty years.

Tennessee has long recognized the learned intermediary doctrine for prescription medicines and medical devices. *See, e.g.*, *Rodriguez v. Strkyer Corp.*, No. 2:08-0124, 2011 WL 31462, at *6 (M.D. Tenn. Jan. 5, 2011); *Smith v. Pfizer, Inc.*, 688 F. Supp. 2d 735, 745 (M.D. Tenn. 2010); *Benson v. Penske Truck Leasing Corp.*, No. 03-2088 Ma/V, 2006 U.S. Dist. LEXIS 18427, at *10 n.3 (W.D. Tenn. March 30, 2006) (dictum); *Isbell v. Medtronic Inc.*, 97 F. Supp. 2d 849, 861 (W.D. Tenn. 1998); *Pittman v. Upjohn Co.*, 890 S.W.2d 425, 429 (Tenn. 1994) (establishing the doctrine in Tennessee); *Nye v. Bayer Cropscience, Inc.*, No. E2008-01596-COA-R3-CV, 2009 WL 3295137, at *12 (Tenn. Ct. App. Oct. 14, 2009) (collecting cases from 1990 to 2001 to show that "[t]he learned intermediary doctrine is well established in Tennessee"); *Johnson v. Settle*, No. M1999-01237-COA-R3-CV, 2001 WL 585093, at *8 (Tenn. Ct. App. June 1, 2001); *King v. Danek Medical, Inc.*, 37 S.W.3d 429, 452–53 (Tenn. Ct. App. 2000). And no case interpreting Tennessee law has recognized a direct-to-consumer-marketing exception to the learned intermediary doctrine. *See, e.g.*, *In re Norplant Contraceptive Prods. Liab. Litig.*, 215 F. Supp. 2d 795, 806–09, 812 (E.D. Tex. 2002) (examining all 50 states, including Tennessee, for learned intermediary exceptions and finding that the direct-to-consumer exception only applied in New Jersey); *Pittman*, 890 S.W.2d at 429.

Plaintiffs assert that since the Tennessee Supreme Court's decision in *Pittman*, the landscape for prescription medicines has changed, implying that Tennessee has done little to revisit its understanding of the learned intermediary doctrine since. (Pls.' Mem. In Supp. of Their Mot. for Partial Summ. J. 20.) To the contrary, Tennessee courts applying Tennessee law

repeatedly have revisited the learned intermediary doctrine since 1994, and have declined to apply a direct-to-consumer exception. *See, e.g.*, *Rodriguez*, 2011 WL 31462, at *6 (medical device to release prescription anesthetic); *Smith*, 688 F. Supp. 2d at 745–46 (Neurotonin prescription); *Isbell*, 97 F. Supp. 2d at 861 (implantable cardiac pacemaker lead); *Johnson*, 2001 WL 585093, at *8 (medicinal acid); *King*, 37 S.W.3d at 452–53 (medical screw).

2. Laws of outlier jurisdictions should not apply to Tennessee

Plaintiffs argue that a direct-to-consumer exception should apply, based on the adoption of such an exception in New Jersey, a ruling by an intermediate Texas court and the rejection of the doctrine in West Virginia. (Pls.' Mem. In Supp. of Their Mot. for Partial Summ. J. 18.) However, rulings from these three states are outliers that are inapplicable in Tennessee. The vast majority of jurisdictions have adopted the learned intermediary doctrine without a direct-to-consumer exception. In addition to Tennessee, thirty-two states plus the District of Columbia have adopted the learned intermediary doctrine without a direct-to-consumer exception through the jurisdiction's highest court or legislature.[3]

[3] *See* **Alabama**: *Walls v. Alpharma USPD*, 887 So.2d 881, 883 (Ala. 2004); **Alaska**: *Shanks v. Upjohn Co.*, 835 P.2d 1189, 1200 & n.17 (Alaska 1992); **Arkansas**: *West v. Searle & Co.*, 806 S.W.2d 608, 613 (Ark. 1991); **California**: *Carlin v. Superior Court*, 920 P.2d 1347, 1354 (Cal. 1996); **Connecticut**: *Hurley v. Heart Physicians, P.C.*, 898 A.2d 777, 783-84 (Conn. 2006); **Delaware**: *Lacy v. G.D. Searle & Co.*, 567 A.2d 398, 400–01 (Del. 1989); **District of Columbia**: *Mampe v Ayerst Labs.*, 548 A.2d 798, 801 & n.6 (D.C. 1988); **Florida**: *E.R. Squibb & Sons, Inc. v. Farnes*, 697 So.2d 825, 827 (Fla. 1997); **Georgia**: *McCombs v. Synthes*, 587 S.E.2d 594, 595 (Ga. 2003); **Hawaii**: *Craft v. Peebles*, 893 P.2d 138, 155 (Hawaii 1995); **Idaho**: *Sliman v. Aluminum Co. of Am.*, 731 P.2d 1267, 1270 (Idaho 1986); **Illinois**: *Happel v. Wal-Mart Stores, Inc.*, 766 N.E.2d 1118, 1127 (Ill. 2002); **Kansas**: *Savina v. Sterling Drug, Inc.*, 795 P.2d 915, 928 (Kan. 1990); **Kentucky**: *Larkin v. Pfizer, Inc.*, 153 S.W.3d 758, 761 (Ky. 2004); **Maryland**: *Rile Aid Corp. v. Levy-Gray*, 894 A.2d 563, 577 (Md. 2006); **Massachusetts**: *Cottam v. CVS Pharmacy*, 764 N.E.2d 814, 820 (Mass. 2002); **Minnesota**: *Mulder v. Parke Davis & Co.*, 181 N.W.2d 882, 885 n.1 (Minn. 1970); **Mississippi**: Miss. Code §11-1-63(c)(ii); *Janssen Pharrnaceutica, Inc. v. Bailey*, 878 So.2d 31, 57 (Miss. 2004); **Missouri**: *Krug v. Sterling Drug, Inc.*, 416 S.W.2d 143, 146–47 (Mo. 1967); **Montana**: *Stevens v. Novartis Pharm. Corp.*, 358 Mont. 474, 492–95 (2010); **Nebraska**: *Freeman v. Hoffman-La Roche, Inc.*, 618 N.W.2d 827, 841–42 (Neb. 2000); **Nevada**: *Allison v. Merck & Co.*, 878 P.2d 948, 958 n.16 (Nev. 1994) (plurality op.), 969 (dissent also following learned intermediary rule); **New York**: *Spensieri v. Lasky*, 723 N.E.2d 544, 549 (N.Y. 1999); **North Carolina**: N.C. Gen. Stat. §99B-5(c); **Ohio**: Ohio Rev. Code §2307.76(c); *Howland v. Purdue Pharma, L.P.*, 821 N.E.2d 141, 146 (Ohio 2004); **Oklahoma**: *Edwards v. Basel Pharm.*, 933 P.2d 298, 300–01 (Okla. 1997); **Oregon**:

Plaintiffs have not alleged any similarity to Tennessee that would make disparate rulings from New Jersey, Texas, and West Virginia more applicable to Tennessee than thirty-three jurisdictions, let alone those of Tennessee itself. *Cf. In re Meridia Prods. Liab. Litig.*, 328 F. Supp. 2d at 812 n.19 (a federal court sitting in diversity must apply the law of the state, and could not apply the New Jersey's direct-to-consumer exception to Ohio law "even if it desired to do so," given the failure of other states to follow New Jersey's lead). Moreover, Tennessee's sister-states in the Sixth Circuit, Kentucky, Michigan, and Ohio, all favor the learned intermediary doctrine without a direct-to-consumer exception.[4]

The New Jersey, Texas, and West Virginia cases by plaintiffs each have a distinct legal landscape, which make them poor analogues for imitation.

In Texas, the case cited by the Plaintiffs in favor of a direct-to-consumer exception, *Centocor v. Hamilton*, 310 S.W.3d 476 (Tex. Ct. App. 2010), is an intermediate appellate court decision currently being appealed to the Texas Supreme Court, and as such, its fate is uncertain. *Hamilton* also was ruled upon in a legal landscape in which the Texas Supreme Court had not spoken unequivocally on the application of the learned intermediary doctrine to prescription medicines, allowing the lower court more latitude for its (not yet affirmed) decision. This is distinct from Tennessee, in which the legal landscape for the learned intermediary

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Oksenholt v. Lederle Labs., 656 P.2d 293, 296-97 (Or. 1982); **Pennsylvania**: *Coyle v. Richardson-Merrell, Inc.*, 584 A.2d 1383, 1385 (Pa. 1991); **South Carolina**: *Madison v. Am. Home Prods. Corp.*, 595 S.E.2d 493, 496 (S.C. 2004); **Utah**: *Schaerrer v Stewart's Plaza Pharmacy, Inc.*, 79 P.3d 922, 928–29 (Utah 2003); **Virginia**: *Pfizer, Inc. v. Jones*, 272 S.E.2d 43, 44 (Va. 1980); **Washington**: *Washington State Physicians Ins. Exch. & Ass'n v. Fisons Corp.*, 858 P.2d 1054, 1061 (Wash. 1993); **Wyoming**: *Rohde v. Smiths Med.*, 165 P.3d 433, 438 (Wyo. 2007).

[4] **Kentucky**: *Larkin v. Pfizer, Inc.*, 153 S.W.3d 758, 761 (Ky. 2004); **Ohio**: Ohio Rev. Code §2307.76(c); *Howland v. Purdue Pharma, L.P.*, 821 N.E.2d 141, 146 (Ohio 2004). Michigan's high court has not explicitly adopted the learned intermediary doctrine without a direct-to-consumer exception outside of dicta, but Michigan's lower courts have done so. *E.g., Mowery v. Crittenton Hosp.*, 400 N.W.2d 633, 637 (Mich. App. 1986).

doctrine as applied to prescription medicines has been established since 1994. *See Pittman*, 890 S.W.2d at 429–30.

In New Jersey, the direct-to-consumer exception was established in 1999 but has received no support in Tennessee. Meanwhile, among federal courts asked to consider a direct-to-consumer exception to the learned intermediary doctrine when applying other state's law, the clear trend has been to explicitly reject the "New Jersey" exception. *See, e.g.*, *In re Diet Drugs Prods. Liab. Litig.*, MDL No. 1203, Nos. 99-20593, 07-20002, 2009 WL 902351, at *2 (E.D. Pa. April 2, 2009) (Missouri law); *Allgood v. GlaxoSmithKline PLC*, Civil Action No. 06-3506, 2008 WL 483574, at *3-4 (E.D. La. Feb. 20, 2008), *aff'd*, 314 Fed. Appx. 701 (5th Cir. 2009) (Louisiana law); *Beale v. Biomet, Inc.*, 492 F. Supp. 2d 1360, 1376–77 (S.D. Fla. 2007) (Florida law); *Cowley v. Abbott Laboratories, Inc.*, 476 F. Supp. 2d 1053, 1060 n.4 (W.D. Wis. Feb. 28, 2007) (North Carolina law); *Heindel v. Pfizer, Inc.*, 381 F. Supp. 2d 364, 378 n.6 (D.N.J. 2004) (Pennsylvania law); *In re Meridia Prods. Liab. Litig.*, 328 F. Supp. 2d 791, 812 n.19 (N.D. Ohio 2004), *aff'd*, 447 F.3d 861 (6th Cir. 2006) (Ohio law); *In re Norplant Contraceptive Prods. Liab. Litig.*, 215 F. Supp. 2d 795, 812 (E.D. Tex. 2002) (rejecting a direct-to-consumer exception when applying the law of every state except New Jersey).

Also, the New Jersey exception differs in at least one important aspect from plaintiffs' proposed exception here. In New Jersey, there is a statutorily-grounded rebuttable presumption that a manufacturer's duty to warn consumers is met when the manufacturer "complies with FDA advertising, labeling and warning requirements." *Perez v. Wyeth Labs. Inc.*, 734 A.2d 1245, 1259; *see also* N.J. Stat. § 2A:58C-4. This presumption is extremely broad: "absent deliberate concealment or non-disclosure of after-acquired knowledge of harmful effects, compliance" with the FDA "should be *virtually dispositive* of such claims." *Perez*, 734 A.2d at

1259 (emphasis added). In this case, plaintiffs have not and cannot show that Centocor failed to comply with FDA regulations in their advertising, labeling, or warning requirements for Remicade®. In other words, the New Jersey exception should not apply in this case, but if it did apply, this presumption of adequacy requires dismissal of plaintiffs' failure-to-warn claims.

Finally, the West Virginia Supreme Court's decision to eliminate the learned intermediary doctrine altogether, *State ex rel Johnson & Johnson Corp. v. Karl*, 647 S.E.2d 899 (W. Va. 2007) is a unique outlier that has not been followed in any other state. And in fact, West Virginia now may be moving toward adoption of the learned intermediary doctrine. In *White v. Wyeth*, 705 S.E.2d 828 (W. Va. 2010), the Supreme Court of Appeals of West Virginia held that "federal regulation of prescriptive drug products attenuates the effect product marketing has on a consumer's prescriptive drug purchasing decision," dismissing *Karl* with a "but see" citation. *Id.* at 838.

B. Plaintiffs were unaffected by any direct-to-consumer marketing in this case

Although plaintiffs say direct-to-consumer marketing should result in an exception to the learned intermediary doctrine, in this case there was no direct-to-consumer marketing.

Plaintiffs do not claim that Ms. Nozinich was ever affected by Centocor's advertising to consumers. Plaintiffs merely claim that Ms. Nozinich was affected by a DVD and brochure produced by Centocor and given to Ms. Nozinich by Dr. Ash. (Plaintiffs' SUF, ¶¶ 19–29, Dkt. Entry No. 87-1; Pls.' Mem. In Supp. of Their Mot. for Partial Summ. J. or in the Alternative Mot. to Strike the Learned Intermediary Defense 3–4, Dkt. Entry 87-14.) These physician-supplied materials do not constitute direct-to-consumer marketing, as they do not displace the physician-patient relationship. *See Thom v. Bristol-Myers Squibb Co.*, 353 F.3d 848,

852 (10th Cir. 2003) ("even if a drug manufacturer provides pamphlets for distribution . . . the patient is expected to place primary reliance on the physician's judgment, and to follow his advice and instructions as to use of the drug" (internal quotation marks omitted)); *In re Norplant Contraceptive Prods. Liab. Litig.*, 955 F. Supp. at 708-09 (informational brochures and videotapes distributed by the physician are an "informational supplement to the physician-patient relationship" and the physician retains a duty to review them); *Spychala v. G.D. Searle & Co.*, 705 F. Supp. 1024, 1033 (D.N.J. 1988); *Banner v. Hoffmann-La Roche, Inc.*, 891 A.2d 1229, 1236 (N.J. Super. App. Div. 2006) (noting that even under *Perez*, "the placement of informational brochures in a physician's office cannot fairly be equated with a course of mass advertising or be deemed direct-to-consumer advertising" so as to supplant the learned intermediary doctrine); *Seley v. G.D. Searle & Co.*, 423 N.E.2d 831, 840 (Ohio 1981) ("a direct relationship between the manufacturer and the patient does not arise as a result of the provision of such brochures"); *Kennedy v. Merck & Co.*, 2003 WL 21658613, at *5 (Ohio App. July 3, 2003).

Thus, even if the Court were to ignore Tennessee law and consider applying a direct-to-consumer exception, the advertising plaintiffs identified is not the type of advertising that supports application of the exception.

C. The learned intermediary doctrine is not a defense and may not be stricken; Plaintiffs must prove Centocor's warnings were inadequate

Plaintiffs characterize the learned intermediary doctrine as an affirmative defense and move for the Court to "strike" it. (Pls.' Mot. for Partial Summ. J. or in the Alternative Mot. to Strike Learned Intermediary Defense, Dkt. Entry 87.) This confuses the nature of the learned intermediary doctrine under Tennessee law and the placement of the burden of proof regarding the adequacy of labeling on plaintiffs.

Plaintiffs claim that "[f]or the learned intermediary doctrine to apply under Tennessee law, 'a warning must contain a full and complete disclosure of the potential adverse reactions to the drug.'" (Pls.' Mem. In Supp. of Their Mot. for Partial Summ. J. or in the Alternative Mot. to Strike the Learned Intermediary Defense 25, Dkt. Entry 87-14.) They further claim that Centocor "cannot rely on the learned intermediary doctrine" if they did not provide adequate warnings to Dr. Ash. (Pls.' Mem. 23.) While this is literally true, plaintiffs misstate their burden of proof, implying that the doctrine does not apply unless Centocor shows that its warning is adequate.

In Tennessee, for manufacturers of prescription medicines and devices, the learned intermediary doctrine simply shifts the manufacturer's duty to warn from consumer to physician. *See, e.g.*, *Pittman*, at 429. It is not an affirmative defense, but a requirement when assessing claims against manufacturers of unavoidably unsafe products such as prescription medicines. *Id.* The burden to show that the warnings were inadequate still falls on plaintiffs as part of the plaintiffs' prima facie failure-to-warn case. "[T]o recover for a failure to warn under the learned intermediary doctrine, a plaintiff must show (1) that the defendant failed to warn the physician of a risk associated with the use of the product not otherwise known to the physician; and (2) that the failure to warn" was a cause of the injury. *E.g.*, *Nye*, 2009 WL 3295137, at *11; *Johnson*, 2001 WL 585093, at *8; *King v. Danek Med., Inc.*, 37 S.W.3d 429, 452 (Tenn. Ct. App. 2000); *Harden v. Danek Med., Inc.*, 985 S.W.2d 449, 451 (Tenn. Ct. App. 1998); *see Spence v. Danek Med., Inc.*, No. 96C-1004, 1998 WL 665760, at *4 (Tenn. Cir. Ct. June 17, 1998) ("a plaintiff must not only show that a manufacturer's warning was inadequate, but that such inadequacy affected the prescribing physicians' use of the product and thereby injured the

plaintiff" (citing *Tiley v. Danek Med., Inc.* No. 3:95 CV 816, 1998 WL 275696 (E.D. Va. May 22, 1998)).

Plaintiffs have the burden to establish that Centocor's warnings to Dr. Ash were inadequate. They have no fact or expert opinion evidence to support such a claim. Under these circumstances, there is nothing to which Centocor must respond.

III. CENTOCOR ADEQUATELY WARNED DR. ASH ABOUT THE RISKS AND BENEFITS OF REMICADE®

As explained in Centocor's summary judgment motion (*See* Defendants' SUF, ¶¶ 5-7, 24; Centocor's Memorandum of Law in Support of Their Summary Judgment Motion at 10), the Remicade® labeling available in 2007 discussed the possible risks of a thromboembolic events, including pulmonary embolism, thrombophlebitis, ischemia and infarction. Dr. Ash was aware of these risks associated with Remicade® at the time she prescribed the medicine to Ms. Nozinich. (Ash Dep. at 36:6-24.) Based on her knowledge of Remicade®, Dr. Ash exercised her independent clinical judgment in prescribing the medicine to alleviate the symptoms of Ms. Nozinich's rheumatoid arthritis. (*Id.*) Remicade® was prescribed properly to Ms. Nozinich and she was benefitting from the medicine as her disease symptoms were improving after the infusions. (*Id.* 22:11-28:2; 40:17-41:14; 47:5-50:16.) And, when the medicine's labeling mentions a possible risk the plaintiff encountered and the prescriber says she was aware of this possibility, no questions of fact exist regarding the adequacy of the warnings. *See Carter v. Danek Med., Inc.*, No. CIV 96-3243-G, 1999 WL 33537317, at *9 (W.D. Tenn. June 3, 1999) (granting summary judgment because the learned intermediary was aware of risks of medical device prior to treating patient with it).

There is no textbook, peer-reviewed paper or reliable study demonstrating an increased risk of pulmonary embolism associated with Remicade®. (Trew Dep., 43:2-9;

Affidavit of Dr. Gary R. Epler ("Epler Aff.") filed on April 7, 2011 (Dkt. Entry No. 84), ¶ 12.) And post-marketing data indicates that the incidence of pulmonary embolism events as well as other thrombotic events is less than what is normally expected in the relevant population groups (*Compare* Trew Dep. 28:13-30:01 *with* Affidavit of Stella Jones, Ph.D. ("Jones Aff.") filed on April 7, 2011 (Dkt. Entry No. 83) ¶¶ 9-10). Indeed, based on the lack of evidence associating Remicade® with pulmonary embolism, FDA removed pulmonary embolism from the Remicade® package insert as a possible "adverse reaction" in April 2010. (Jones Aff. ¶ 10; Epler Aff. ¶ 12.) All of this negative evidence – that is, proof of a lack of an association – is contained the PSURs referenced in plaintiffs' motion.

That Centocor received reports of pulmonary embolism and other thromboembolic events since the medicine was first marketed is not meaningful to an inquiry regarding the adequacy of labeling, unless the number of reports exceeds what would be normally expected in the population receiving the medicine. *See Pittman*, 890 S.W.2d at 429 (listing criteria for an adequate warning and stating that "[w]arnings concerning prescription drugs generally are adequate when they contain a full and complete disclosure of potential adverse reactions to the drug.") Here, in some of the patient populations for whom Remicade® is prescribed, the incidence of thromboembolism can be as high as 6%. (Trew Dep. 28:13-29:14 (in Crohn's patients the incidence of thromboembolic events may be 500 to 600 times higher than in the general healthy population)) The currently available data suggests the incidence associated with Remicade® is a small fraction of this incidence rate. (Jones Aff. ¶¶ 9-10.) Therefore, there is no basis to even suggest that there is an increased risk of pulmonary embolism or thromboembolism associated with Remicade®. Under these circumstances, the fact

that pulmonary embolism was included in the Remicade® labeling prior to 2010, reflects a very conservative – full disclosure -- approach by Centocor and FDA.

IV. WITHOUT EXPERT PROOF, PLAINTIFFS' FAILURE-TO-WARN CLAIM MUST BE DISMISSED

To avoid summary judgment, plaintiffs were required to produce admissible expert proof regarding the adequacy of the Remicade® warnings. *See Scelta v. Boehringer Ingelheim Pharms., Inc.*, 404 F. App'x 92, 94 (8th Cir. 2010) (applying Florida law, finding that plaintiff failed to produce a genuine issue of fact because he did not produce expert testimony on adequacy of warning label); *Miller v. ALZA Corp.*, No. 3:08-cv-402, 2010 WL 5287514, at *14 n.10 (S.D. Ohio Dec. 17, 2010) (citing *White v. Wyeth Lab., Inc.*, Case Nos. 52108, 2564, 1987 WL 14953, at *5 (Ohio App. July 30, 1987) (a plaintiff needs to present expert medical testimony regarding adequacy of warning of medical risks); *Mason v. Smithkline Beecham Corp.*, No. 05-1252, 2010 WL 2697173, at *5 (C.D. Ill. July 7, 2010) (whether manufacturer knew of the risk of a medicine and whether that risk was enough to be included on a label is "beyond a lay juror's expertise; therefore, expert testimony is required to show that the label was inadequate."); *Aaron v. Wyeth*, No. 2:07cv927, 2010 WL 653984, at *9 (W.D. Pa. Feb. 19, 2010) (referring to plaintiffs' claims, "Generally, the adequacy of a warning in prescription drug cases must be proven by expert testimony."); *see also Montagnon v. Pfizer, Inc.*, 584 F. Supp. 2d 459, 463 (D. Conn. 2008) (failing to find warning inadequate because, while expert testimony might not be required as a matter of law, neither the court nor the jury could draw conclusions about studies that might supersede the determinations of FDA labeling). Plaintiffs produced no expert that opined on the adequacy of the Remicade® labeling. Because they needed expert proof to survive summary judgment (and they do not have it), plaintiff's failure-to-warn claims must be dismissed. *See Scelta*, 404 F. App'x at 94.

As set forth in Centocor's summary judgment motion, Dr. Trew—plaintiff's only "expert"—admitted he has no expertise in pharmaceutical labeling. To this end, Dr. Trew testified he had no experience in the development and evaluation of labeling for a pharmaceutical product. Nor does he have any regulatory experience with respect to a product like Remicade®. (Trew Dep., 119:23-25, 153:3-8). Accordingly, even if he disclosed an opinion (which plaintiffs did not do), any warning opinion from Dr. Trew is inadmissible. Moreover, the Court's grant of Centocor's *in limine* motion to exclude Dr. Trew at this point makes any further discussion about what Dr. Trew could or could not say moot.

Not one of the documents plaintiffs attach or reference constitute any opinion, let alone an opinion that the Remicade® labeling available in 2007 was inadequate. To the contrary, the documents show that the prescribing information incorporated the "state of the art" and was based on complete information. Though it evolved just like labeling for all medicines, the Remicade® labeling always accurately and sufficiently reflected the known potential risks associated with using Remicade®, including thrombotic and pulmonary events, as assessed through Centocor's monitoring of safety data with reliable methodologies. (Defendants' SUF, ¶¶ 5-8; Defendants' Response to Plaintiffs' Statement of Material Facts, ¶¶ 43, 44, 50, 51, 57, 61.) And when labeling meets this standard, it is adequate as a matter of law. *See Ackermann v. Wyeth Pharms.*, 526 F.3d 203, 208 (5th Cir. 2008) (applying Texas law, "[i]n prescription drug cases involving the intermediary doctrine, when a warning specifically mentions the circumstances complained of, the warning is adequate as a matter of law"); *Meridia.*, 447 F.3d at 867 (warning label that medicine substantially increased blood pressure was adequate as a matter of law that drug could cause high blood pressure and related consequences); *Wright v. Abbott Labs.*, 259 F.3d 1226, 1233 (10th Cir. 2001) ("Under Kansas law, a plaintiff cannot prevail

against a prescription drug manufacturer in a failure to warn case where the manufacturer warned the 'learned intermediary' of the drug's inherent risks."); *Fane v. Zimmer, Inc.*, 927 F.2d 124, 130 (2d Cir. 1991) ("[b]ecause the warnings provided specific information on the risks associated with use of the . . . device" and because learned intermediary was aware of those risks, the warnings were adequate as a matter of law); *Pittman*, 890 S.W.2d at 430 (warnings that medicine could cause mild and severe hypoglycemia were adequate as a matter of law to warn of danger of hypoglycemia when consumed by member of patient's family).

V. DTC AND OTHER MARKETING ACTIONS HAVE NOTHING TO DO WITH THIS CASE

To use "marketing documents" affirmatively or in opposition to a summary judgment motion, plaintiffs must demonstrate not only that the materials influenced Dr. Ash's decision to prescribe Remicade®, but that Dr. Ash *actually relied* on such materials. *See, e.g., Haynes v. Am. Motors Corp*., 691 F.2d 1268. 1270-71 (8th Cir. 1982). Absent a showing of reliance, plaintiffs' failure to warn claims based on these materials fail as a matter of law. *See, e.g., Parks v. Danek Medical, Inc.*, No. 2:95 CV 206, 1999 WL 1129706, at *11 (N.D. Ind. Jun. 17, 1999); *Valente v. Sofamor, S.N.C.*, 48 F. Supp. 2d 862, 873 (E.D. Wis. 1999) (plaintiffs failed to make prima facie case because they could not show reliance); *see also Prohaska v. Sofamor, S.N.C.*, 138 F. Supp. 2d 422, 446 (W.D.N.Y. 2001) (plaintiffs need to prove that treating physician relied on specific false statement by defendants, and physician made own independent judgment); *Alexander v. Smith & Nephew, P.L.C.*, 90 F. Supp. 2d 1225, 1235 (N.D. Ok. 2000) (plaintiff needs to submit evidence of physicians' reliance of defendant's representations); *In re Norplant Contraceptive Prod. Liab. Litig.*, No. MDL 1038, 1997 WL 81092, at *1 (E.D. Tex. Feb. 21, 1997) ("[a]bsent evidence that the physicians were exposed to

the above listed materials, the court finds that the promotional materials are not relevant evidence."). Plaintiffs have not and cannot satisfy this burden.

The evidence is undisputed that Dr. Ash exercised her independent judgment prescribing Remicade® for Ms. Nozinich and was not co-opted or influenced by Centocor. (*See* Ash Dep., 22:11-28:2; 40:17-41:14; 47:5-50:16; Trew Dep., 115:21-116:8, 120:5-21). Dr. Ash testified that her knowledge and understandings about Remicade® came from sources other than Centocor. (Ash Dep., at 53:10-54:3). And while it is not legally relevant, plaintiffs themselves were not "influenced" by some marketing campaign to request Remicade®. Ms. Nozinich did not see any Remicade® advertisement of any kind prior to Dr. Ash mentioning the medicine to Ms. Nozinich for the first time.

There simply is no connection between any marketing effort by Centocor and Dr. Ash's decision to prescribe Remicade® for Ms. Nozinich. Under these circumstances, the memos and documents referenced by plaintiffs are irrelevant to Centocor's summary judgment motion as well as plaintiffs' partial motion. *See Nix v. O'Malley*, 160 F.3d 343, 347 (6th Cir. 1998).

VI. FOREIGN REGULATORY DOCUMENTS ARE NOT ADMISSIBLE

In their motion, plaintiffs cite questions raised by the Swiss equivalent of FDA as somehow being relevant to Dr. Ash's decisions regarding her care and treatment of Ms. Nozinich. (*See* Plaintiffs' SUF, ¶¶ 50-55) The Sixth Circuit has made it clear, however, that foreign regulatory documents are not admissible to prove an inadequacy in U.S. labeling or as "notice" evidence. *See Meridia*, 447 F.3d at 867; *see also In re Baycol Prods Litig.*, 532 F. Supp. 2d 1029, 1054 (D. Minn. 2007) (foreign regulatory actions not admissible for any purpose); *In re Seroquel Prods. Liab. Litig.*, 601 F. Supp. 2d 1313, 1314-18 (M.D. Fla. 2009)

(same); *In re Trasylol Prods. Liab. Litig.-MLD-1928*, 709 F. Supp. 2d 1323, 1336 (S.D. Fla. 2010) (same).

Varying medical practices, cultural norms and health care management schemes, clearly impact regulatory decisions. These factors also affect decisions on the content of product labels in various countries. All these differences demonstrate that the facts and circumstances surrounding the foreign regulatory documents are not substantially similar to FDA decision-making. *See Meridia*, 447 F.3d at 867. Therefore, these types of documents and interactions are excluded from consideration when the merits of a case are evaluated. *See Bunting v. Sea Ray, Inc.*, 99 F.3d 887, 891-92 (8th Cir. 1996) (district court did not abuse its discretion in excluding test results where "the setting of the tests were too dissimilar to the facts" of the case); *Hurt v. Coyne Cylinder Co.*, 956 F.2d 1319, 1327 (6th Cir. 1992) (foreign standards not admissible in product liability case).

Plaintiffs, as the proponent of the foreign regulatory materials, bear the burden of showing the relevancy of these exhibits. Therefore, unless plaintiffs produced proof that Dr. Ash saw and relied on the foreign regulatory materials, any arguments relating to the foreign regulatory materials cannot be considered. *See Haynes*, 691 F.2d at 1270-71; *Vroman v. Sears, Roebuck & Co.*, 387 F.2d 732, 734, 738 (6th Cir. 1967) (commercials that were not seen by plaintiff were not admissible to constitute evidence of lack of a warning); *Salmon v. Parke, Davis & Co.*, 520 F.2d 1359, 1362 (4th Cir. 1975); *Parks*, 1999 WL 1129706, at *11; *Valente*, 48 F. Supp. 2d. at 873. Because plaintiffs cannot connect the Swiss Medic communications with Dr. Ash, they are inadmissible under Federal Rules of Evidence 401 and 403.

Even if the Court looks at Centocor's submissions to SwissMedic, the outcome here is no different. Dr. Ash was provided prescribing information and data from studies that

identified pulmonary embolism as a possible adverse event, but described this risk as occurring at or near the same frequency as patients receiving a placebo. (Ash Dep., 36:12-17). The conclusion to the submission to SwissMedic is as follows:

> [Thromboembolic events] TEE, including PE, can be expected to occur in the population treated with infliximab. When an adequate medical history is available, these events often have confounding factors associated with the event. When considering confounding factors and comparing reporting rates in clinical trials and registries with population incidence rates, there does not appear to be an excess of PE reported in patients treated with infliximab. In those cases reported, there did not seem to be particular causality associated with infliximab exposure. Thrombophlebitis is included in the local labels. This analysis indicates that the current labelling is sufficient.

(*See* CE 01607193-95 at CE 01607195, attached to Defendants' Notice of Filing Centocor Documents Under Seal as **Exhibit H**, filed concurrently herewith.)

The message and analysis provided to Dr. Ash and SwissMedic was the same. And this message and analysis was "sufficient" and adequate to characterize the possible risks and benefits of Remicade®.

CONCLUSION

For all the foregoing reasons, plaintiffs' partial summary judgment motion should be denied and Centocor's summary judgment motion should be granted.

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Respectfully Submitted:

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CERTIFICATE OF SERVICE

The undersigned hereby certifies that on the 6th day of May, 2011, a copy of the foregoing was filed electronically. Notice of this filing will be sent by operation of the Court's electronic filing system to all parties indicated on the electronic filing receipt. Parties may access this filing through the Court's electronic filing system.

/s/ Clarence A. Wilbon